

## ***Remarks***

### ***I. Status of the Claims***

By the forgoing amendments, claims 28-31, 34-38, 41-44, 48-56, 61-62, 78-80 and 83-85 have been cancelled without prejudice thereto or disclaimer thereof. Applicants reserve the right to prosecute the subject matter of these claims in one or more continuing applications. Also by the foregoing amendments, new claims 86-110 are sought to be added. Support for these new claims can be found throughout the specification, particularly in claims 28-85 as originally filed; and in the specification throughout the Examples and in the description, for example at page 34, paragraph 137, at page 43, paragraph 166, and at page 58, paragraph 226.

Hence, these amendments do not add new matter, and their entry and consideration are respectfully requested. Upon entry of the foregoing amendments, claims 1-27, 32, 33, 39, 40, 45-47, 57-60, 63-77, 81, 82 and 86-110 are pending in the application, with claims 1, 11, 21, 63 and 86-89 being the independent claims.

### ***II. Summary of the Office Action***

In the Office Action dated February 7, 2003, the Examiner has made two objections to, and eight rejections of, the claims. Based on the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

***III. The Objection to Claims Directed to Non-elected Species is Accommodated***

In the Office Action at page 2, the Examiner has objected to claims 28-30, 34, 36-38, 41-44, 48-56, 61, 62, 78-80, and 83-85 as reading, at least in part, on non-elected species. Applicants respectfully traverse this objection. However, to expedite prosecution and not in acquiescence to this objection, claims 28-30, 34, 36-38, 41-44, 48-56, 61, 62, 78-80, and 83-85 have been cancelled, thus rendering this objection moot. Applicants further note that new claims 86-110 are not drawn to non-elected species; hence, this objection should not be asserted against the new claims entered above.

***IV. The Objection to Claims of Improper Form is Accommodated***

In the Office Action at page 2, the Examiner has objected to claims 48-56, 79, 80 and 83-85 as being in improper form, for presenting multiple dependent claims that depend from other multiple dependent claims. By the forgoing amendments, and for reasons unrelated to this objection, claims 48-56, 79, 80 and 83-85 have been cancelled, thus rendering this objection moot. Applicants note that new claims 86-110 do not contain improper multiple dependencies; hence, this objection should not be asserted against the new claims entered above.

***V. The Rejection under 35 U.S.C. § 112, Second Paragraph***

In the Office Action at page 3, the Examiner has rejected claims 34-38, 41-44, 61, 62 and 78 under 35 U.S.C. § 112, second paragraph, for failing to particularly point

out and distinctly claim the subject matter which Applicants regard as the invention. By the foregoing amendments, claims 34-38, 41-44, 61, 62 and 78 have been cancelled, rendering this rejection moot.

Applicants also respectfully assert that new claims 86-89, and the remaining claims that depend therefrom, should not be rejected on these same grounds, since the recitation of “a core particle” in section (a)(i) of claims 86-89 provides the antecedent basis for the recitation of “said core particle” in section (a)(ii) of these same claims. Hence, this rejection has been overcome, and Applicants therefore respectfully request that the rejection under 35 U.S.C. § 112, second paragraph, be reconsidered and withdrawn.

***VI. The Rejection Under 35 U.S.C. § 102(e) Over Birkett***

In the Office Action at page 3, the Examiner has rejected claims 28-31, 61 and 62 under 35 U.S.C. § 102(e), as being unpatentable over Birkett *et al.* (document “A” cited on the Form PTO-982 attached to Paper No. 11; hereinafter “Birkett”). By the foregoing amendments, claims 28-31, 61 and 62 have been cancelled, rendering this rejection moot.

Applicants also respectfully assert that new claims 86-89, and the remaining claims that depend therefrom, should not be rejected on these same grounds. Claims 86-89 recite, in relevant part, the use of core particles having particular amino acid characteristics (*i.e.*, having polypeptides that are based upon SEQ ID NO:134 or SEQ ID NO:158, but in which the cysteine residues at positions 48 and 107 in SEQ ID NO:134, or at positions 48 and 110 in SEQ ID NO:158 (which correspond to positions 48 and 107 in SEQ ID NO:134), are deleted or substituted with another amino acid. Applicants respectfully assert that Birkett does not disclose each and every element of the claims as currently presented. Specifically,

Birkett does not disclose the use of core particles in which the cysteine residues at positions 48 and 107 of SEQ ID NO:134 (or at positions 48 and 110 of SEQ ID NO:158) are either deleted or substituted with another amino acid. Instead, the sequence in Birkett that is referred to by the Examiner in making this rejection contains a cysteine at position 48, and does not contain the Gly-Gly-Lys-Gly-Gly substitution for amino acids 79 and 80 of SEQ ID NO:134 to result in SEQ ID NO:158.

Under 35 U.S.C. § 102, a claim can only be anticipated if every element in the claim is expressly or inherently disclosed in a single prior art reference. *See Kalman v. Kimberly Clark Corp.*, 713 F.2d 760, 711 (Fed.Cir. 1983), *cert. denied*, 465 U.S. 1026 (1984). As noted above, Birkett clearly does not disclose a virus-like particle that is a dimer or a multimer of a polypeptide having the amino acid sequence characteristics recited in present claims 86-89. Therefore, Birkett does not disclose every element of the presently claimed invention, and in view of *Kalman*, Birkett cannot and does not anticipate the presently claimed invention.

#### ***VII. The Rejection Under 35 U.S.C. § 103(a) Over Birkett***

In the Office Action at pages 4-5, the Examiner has rejected claims 41, 42, 44, 48-56, 79 and 80 under 35 U.S.C. § 103(a) as being unpatentable over Birkett. By the foregoing amendments, claims 41, 42, 44, 48-56, 79 and 80 have been cancelled, rendering this rejection moot.

Applicants also respectfully assert that new claims 86-89, and the remaining claims that depend therefrom, should not be rejected on these same grounds. As discussed above, claims 86-89 recite, in relevant part, the use of core particles having particular amino acid

characteristics (*i.e.*, having polypeptides that are based upon SEQ ID NO:134 or SEQ ID NO:158, but in which the cysteine residues at positions 48 and 107 in SEQ ID NO:134, or at positions 48 and 110 in SEQ ID NO:158 (which correspond to positions 48 and 107 in SEQ ID NO:134), are deleted or substituted with another amino acid. For reasons noted above, which are reiterated and incorporated herein by reference, Birkett is seriously deficient as a reference upon which to base a *prima facie* case of obviousness. Specifically, Birkett does not disclose, suggest, or otherwise contemplate the use of a virus-like particle that is a dimer or a multimer of a polypeptide having the amino acid sequence characteristics recited in present claims 86-89.

In proceedings before the Patent and Trademark Office, the Examiner bears the burden of establishing a *prima facie* case of obviousness based upon the prior art. *See In re Piasecki*, 223 USPQ 785, 787-88 (Fed. Cir. 1984). The Examiner can satisfy this burden only by showing some objective teaching in the prior art, or that knowledge generally available to one of ordinary skill in the art, would lead that individual to combine the relevant teachings of the references in such a way as to produce the invention as claimed, *see In re Fine*, 5 USPQ2d 1596,1598 (Fed. Cir. 1988). In the present case, the Examiner's burden has not been satisfied since such a reason, suggestion, or motivation is completely lacking in the disclosure of Birkett. Specifically, the Examiner has pointed to no disclosure or suggestion in Birkett that would have motivated one of ordinary skill to have modified the sequence disclosed in Birkett so as to make and use the presently claimed core particles. Absent such suggestion and motivation, the claimed invention cannot be held to be obvious over Birkett.

***VIII. The Rejection Under 35 U.S.C. § 103(a) Over Birkett in View of Pasek***

In the Office Action at pages 4-5, the Examiner has rejected claims 34, 35, 37, 41, 42, 44, 48-56, 61, 62, 79 and 80 under 35 U.S.C. § 103(a) as being unpatentable over Birkett in view of Pasek *et al.* (document “V” cited on the Form PTO-892 attached to Paper No.11; hereinafter “Pasek”). By the foregoing amendments, claims 34, 35, 37, 41, 42, 44, 48-56, 61, 62, 79 and 80 have been cancelled, rendering this rejection moot.

Applicants also respectfully assert that new claims 86-89, and the remaining claims that depend therefrom, should not be rejected on these same grounds. For reasons noted above, which are reiterated and incorporated herein by reference, Birkett is seriously deficient as a reference upon which to base a *prima facie* case of obviousness. Specifically, Birkett does not disclose, suggest, or otherwise contemplate the use of a virus-like particle that is a dimer or a multimer of a polypeptide having the amino acid sequence characteristics recited in present claims 86-89. Indeed, the Examiner correctly notes that the core sequence in Birkett differs from SEQ ID NO:158 of the present invention. However, the Examiner contends that the skilled artisan would have been motivated to substitute the Hepatitis B sequence disclosed in Pasek for the sequence utilized in Birkett to generate the claimed invention. Applicants respectfully disagree with this contention. The Examiner further asserts that Pasek discloses a Hepatitis B core sequence “which is identical to SEQ 95 [*sic*; SEQ ID NO:158] except for a 5-amino acid insert at residue 78 . . . .” Office Action at page 5, line 14. Applicants note that, as the Examiner has stated, the amino acid sequence disclosed in Pasek is *not* identical to SEQ ID NO:158 disclosed in the present application. Applicants therefore submit that Pasek does not cure the deficiencies in Birkett, as neither the sequence disclosed in Birkett nor the sequence disclosed in Pasek are identical to SEQ

ID NO:158.

Moreover, as noted above, claims 86-89 recite, in relevant part, the use of core particles having particular amino acid characteristics (*i.e.*, having polypeptides that are based upon SEQ ID NO:134 or SEQ ID NO:158, but in which the cysteine residues at positions 48 and 107 in SEQ ID NO:134, or at positions 48 and 110 in SEQ ID NO:158 (which correspond to positions 48 and 107 in SEQ ID NO:134), are deleted or substituted with another amino acid. As discussed above, Birkett does not disclose or suggest such core particles, and these deficiencies are not cured by the disclosure of Pasek which does not suggest core particles in which the cysteine residues at positions 48 and 107 of SEQ ID NO:134 (or at positions 48 and 110 of SEQ ID NO:158) are either deleted or substituted with another amino acid. Hence, one of ordinary skill would have found no disclosure or suggestion that would have motivated one of ordinary skill to have modified the HBV sequence of Birkett with the sequence of Pasek, in order to make and use the core sequences recited in the present claims. Absent such suggestion and motivation, the cited references may not be properly combined to render the claimed invention obvious. *See In re Fine*, 5 USPQ2d 1596,1598 (Fed. Cir. 1988). Thus, the burden required to sustain a *prima facie* case of obviousness cannot be met using the disclosures of Birkett and Pasek.

The Examiner is also reminded that it is axiomatic that, in order to support a *prima facie* case of obviousness, the prior art must suggest making the *specific* molecular modifications necessary to achieve the claimed invention. *See In re Deuel*, 51 F.3d 1552, 1558 (Fed. Cir. 1995); *In re Lahu*, 747 F.2d 703, 705 (Fed. Cir. 1984) (“[t]he prior art must provide one of ordinary skill in the art the motivation to make the proposed molecular modifications needed to arrive at the claimed compound.”). That is, simply because “one

can conceive a general process in advance for preparing an *undefined* compound [*e.g.*, a core particle comprising a ‘Hepatitis B amino acid sequence’] does not mean that a claimed *specific* compound [*e.g.*, a core particle comprising SEQ ID NO:134 or SEQ ID NO:158 (or portions thereof) which is modified so that the cysteine residues at positions 48 and 107 of SEQ ID NO:134 (or 48 and 110 of SEQ ID NO:158) are either deleted or substituted with another amino acid’] was precisely envisioned and therefore obvious.” *Deuel* at 1559. Thus, in order for either Birkett and/or Pasek to be suitable as references upon which to base a *prima facie* case of obviousness, there must be, at a minimum, a teaching or suggestion in these references that would have compelled one of ordinary skill in the art to include in their core particles a polypeptide having the amino acid characteristics recited in claims 86-89, which are substantially different from those of the HBV sequences disclosed in these references. As noted above, such a teaching or suggestion is wholly lacking in both Birkett and Pasek. Therefore, these documents are seriously deficient as a primary references (particularly in view of the holdings in *Deuel* and *Lalu*), and cannot support a *prima facie* case of obviousness of the presently claimed invention.

***IX. The Rejection Under 35 U.S.C. § 103(a) Over Birkett in View of Neurath***

In the Office Action at page 6, the Examiner has rejected claims 43 and 78 under 35 U.S.C. § 103(a) as being unpatentable over Birkett in view of Neurath *et al.* (document “B” cited on the Form PTO-892 attached to Paper No.11; hereinafter “Neurath”). By the foregoing amendments, claims 43 and 78 have been cancelled, rendering this rejection moot.

Applicants also respectfully assert that new claims 86-89, and the remaining claims that depend therefrom, should not be rejected on these same grounds. For reasons noted



above, which are reiterated and incorporated herein by reference, Birkett is seriously deficient as a reference upon which to base a *prima facie* case of obviousness. Specifically, Birkett does not disclose, suggest, or otherwise contemplate the use of a virus-like particle that is a dimer or a multimer of a polypeptide having the amino acid sequence characteristics recited in present claims 86-89. These deficiencies in Birkett are not cured by the disclosure of Neurath, which provides no suggestion or disclosure of the use of core particles having the amino acid sequence characteristics recited in present claims 86-89. Hence, under *Piasecki* and *Fine*, Birkett and Neurath cannot be properly combined in the attempt to render obvious the present claims.

**X.     *The Rejection Under 35 U.S.C. § 103(a) Over Birkett in View of Pasek, Mark and Zhou***

In the Office Action at pages 6 and 7, the Examiner has rejected claims 36 and 38 under 35 U.S.C. § 103(a) as being unpatentable over Birkett in view of Pasek, and further in view of Mark *et al.* (document "C" cited on the Form PTO-892 attached to Paper No.11; hereinafter "Mark") and Zhou *et al.* (document "Z" cited on the Form PTO-892 attached to Paper No. 11; hereinafter "Zhou"). By the foregoing amendments, claims 43 and 78 have been cancelled, rendering this rejection moot.

Applicants also respectfully assert that new claims 86-89, and the remaining claims that depend therefrom, should not be rejected on these same grounds. For reasons discussed above (which are reiterated and incorporated by reference herein by reference), Birkett, alone or in combination with Pasek, does not disclose, suggest or otherwise contemplate the presently claimed invention, since these references do not disclose, suggest or otherwise

contemplate a core particle having the amino acid sequence characteristics recited in the claims as currently presented. Hence, Birkett and Pasek are seriously deficient as references upon which to attempt to base a *prima facie* case of obviousness.

These deficiencies in Birkett and Pasek are not cured by the disclosures of Mark or Zhou, alone or in combination, neither of which provides any suggestion or disclosure of the use of core particles having the amino acid sequence characteristics recited in present claims 86-89. Hence, under *Piasecki* and *Fine*, Birkett, Pasek, Mark and Zhou cannot be properly combined in the attempt to render obvious the present claims.

***XII. The Rejection Under 35 U.S.C. § 103(a) Over Birkett in View of Davis***

In the Office Action at page 7, the Examiner has rejected claims 83-85 under 35 U.S.C. § 103(a) as being unpatentable over Birkett in view of Davis *et al.* (document "N" cited on the Form PTO-892 attached to Paper No.11; hereinafter "Davis"). By the foregoing amendments, claims 83-85 have been cancelled, rendering this rejection moot.

Applicants also respectfully assert that new claims 86-89, and the remaining claims that depend therefrom, should not be rejected on these same grounds. For reasons discussed above (which are reiterated and incorporated by reference herein by reference), Birkett does not disclose, suggest or otherwise contemplate the presently claimed invention, since these references do not disclose, suggest or otherwise contemplate a core particle having the amino acid sequence characteristics recited in the claims as currently presented. Hence, Birkett is seriously deficient as a reference upon which to attempt to base a *prima facie* case of obviousness. These deficiencies in Birkett are not cured by the disclosure of Davis, which provides no suggestion or disclosure of the use of core particles having the amino acid

sequence characteristics recited in present claims 86-89. Hence, under *Piasecki* and *Fine*, Birkett and Davis cannot be properly combined in the attempt to render obvious the present claims.

### ***XIII. The Double Patenting Rejection***

In the Office Action at pages 7-8, the Examiner has provisionally rejected claims 28-31, 34-38, 41-44, 48-56, 61, 62, 78-80 and 83-85 under the judicially created doctrine of obviousness-type double-patenting, as allegedly being patentably indistinct from claims 50, 51, 54, 57 and 58 in copending Application No. 09/449,631. By the foregoing amendments, claims 28-31, 34-38, 41-44, 48-56, 61, 62, 78-80 and 83-85 have been cancelled, thus rendering this rejection moot.

### ***IX. Conclusion***

All of the stated grounds of objection and rejection have been properly traversed. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn.

Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt entry and consideration of the present Amendment and Reply, and allowance of all pending claims, are earnestly solicited.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

A handwritten signature in dark ink, appearing to read "Brian J. Del Buono", with a long horizontal flourish extending to the right.

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